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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/692,542	10/24/2003	John P. Yardley	AM100159 P1	1126

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EXAMINER	
ROBINSON, BINTA M	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 12/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/692,542	YARDLEY ET AL.	
	Examiner	Art Unit	
	Binta M. Robinson	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-22 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-22 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 10/24/03.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4 ,10, 22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating depression, stress urinary incontinence, bulimia nervosa, Alzheimer's disease, Parkinson's disease, senile dementia, generalized anxiety disorder, cocaine and alcohol addiction, schizophrenia, panic disorder, post traumatic stress disorder, attention deficit disorder with and without hyperactivity, epilepsy, postherpetic neuralgia, and certain forms of pain, such as some types of headache, chronic radicular back pain, and fibromyalgia, does not reasonably provide enablement for a method of treating all disorders of the central nervous system in a mammal such as amnesia, Shy-Drager Syndrome, borderline personality disorder, late luteal phase dysphoric disorder, Gilles de la Tourette Syndrome, vasomotor flushing, chronic fatigue syndrome, all forms of pain, all forms of urinary incontinence, all neurodegenerative disorders, or a method for enhancing cognition in a mammal, comprising providing to a mammal in need thereof a pharmaceutically effective amount of a compound of formula I. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Enhancing cognition is a not the treatment of a specific disease. The

enhancing of cognition must be related to a disease that needs to be improved and this disease needs to be recited.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The Nature of the Invention

The nature of the invention is the use of compounds of formula I for treating central nervous system disorders as well as inhibiting cognition in a mammal.

The state of the prior art

The state of the prior art is that venlafazine derivatives have been used in treating hypothalamic amenorrhea in non-depressed women (See 5506270, Reference A) and in general is known as a potent inhibitor of monoamine neurotransmitter uptake, a mechanism associated with reproductive function. (See 5506270, Reference A). Venlafaxine has been used in treating generalized anxiety disorder (see Hcaplus 134:65678), anxiety disorders (See Hcaplus 132:44393), in treating depression (See PubMed ID 7729333. The effect of venlafaxine on the

mechanism of action neurotransmitters is uncertain. It is believed that venlafaxine's mechanism of action is related to potent inhibition of the uptake of the monoamine neurotransmitter serotonin and orepinephrine. (See 5506270, See Reference A). Evidence on the point is relatively scanty at the present time as to whether venlafaxine has a role in the management of chronic fatigue syndrome, loss of libido and/or erectile dysfunction (See Hcaplus 129:239318.). There has been insufficient data for an assessment of the evidence of effectiveness of venlafaxine on some types of neuropathic pains. See PubMed ID: 16034979. Additional randomized, controlled trials are necessary to fully elucidate the role of venlafaxine in the treatment of chronic pain; currently, no antidepressants, including venlafaxine , are approved for the treatment of chronic pain syndromes. See PubMed ID: 1512896. Racemic Venlafaxine has adverse physiological affects. See (US Patent 6441048, Column 2, lines 27-38).

The Predictability or lack of in the art

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In the absence of a showing of any biological assays of the compounds claimed on the specific diseases claimed, and on enhancing cognition, one of skill in the art is unable to fully predict possible results from the administration of the compound.

The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The amount of direction or guidance present

The direction present in the instant specification is that the compounds of claim 1 can enhance cognition and treat the diseases of the central nervous system that are claimed. However, the specification provides no experimental assays which demonstrate the pharmacological activity of these compounds on enhancing cognition or on the specific diseases claimed.

The presence or absence of working examples

The specification provides no experimental assays which demonstrate the pharmacological activity of these compounds on enhancing cognition or on the specific diseases claimed.

There are no working examples for any diseases listed in the specification or claimed. Also, the compounds which are disclosed in the specification have no pharmacological data regarding the treatment of disease.

The breadth of the claims

The breadth of the claims is that the compound can treat any central nervous system disease in a mammal or enhance cognition in a mammal.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what claimed diseases would be benefited by treatment with a compound of claim 1.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound for the treatment of any central nervous system disease or enhancing cognition. As a result necessitating one of skill to perform an exhaustive search for which central nervous system diseases can be treated by the compound of claim 1 in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which central nervous system diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 3, 4-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. In claim 1, lines 7-8, and everywhere else throughout claims 2, 3, 4-21, the phrase "salts or hydrates thereof" is indefinite. Applicant is claiming a compound claim yet makes reference to this compound existing in salts or hydrates thereof. A compound only exists in singular form not plural form. Is the applicant claiming a compound or a composition which consists of at least 2 compound ingredients? Additionally, it is unclear and indefinite as to what hydrates the applicant is claiming since these hydrates are not further delineated in the specification.

B. Claim 18 recites the limitation "urinary incontinence or chronic obstructive pulmonary disease" in line 2. There is insufficient antecedent basis for this limitation in the claim. Urinary incontinence has diverse etiologies (See

Hcaplus 142:290514) and is not always a central nervous system disorder. Chronic obstructive pulmonary disease is also not a central nervous system disorder.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6441048 because of the 102 (e) date of the patent, and further in view of Bundgaard.

US 6441048 claimed the drug of the instant compound, O-desmethylvenlafaxine, the pharmaceutical composition containing this compound and a method of treating affective disorders including but not limited to attention deficit disorder, attention deficit disorder without hyperactivity, cerebral function disorders including, but not limited to senile dementia, Parkinson's disease, Alzheimer's disease, amnesia/amnestic syndrome, autism, schizophrenia, chronic pain, pre-menstrual syndrome, anxiety, eating disorders, migraines, obsessive compulsive disorder, substance abuse with the drug. See O-desmethylvenlafaxine and the uses of this compound at column 2. The instant compound in which the hydroxyl group on the phenyl moiety of the compound, is protected with an ether, is the prodrug of the '048 compound which has the free hydroxyl group on the phenyl moiety of the compound. (See Bundgaard, page

6). The difference between the '048 drug and the instantly claimed prodrug is that instead of the free hydroxyl moiety on the phenyl portion of the compound, the instant claim is drawn to an ether prodrug of the hydroxyl functional group. Ethers can be prodrugs for phenol compounds. (See Bundgaard, page 5). One having ordinary skill in the art is deemed to be aware of all the prodrug forms conventional to the art. Since a prodrug is a pharmaceutical formulation for delivery of a drug and dependent on the drug for utility, prodrugs are prima facie obvious over the conventional drug.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (571) 272-0692. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703)308-4242, (703)305-3592, and (703)305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)-272-1600.

Cecilia J. Tsang
Supervisory Patent Examiner
Technology Center 1600